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KIRK-OTHMER

ENCYCLOPEDIA OF CHEMICAL TECHNOLOGY

THIRD EDITION

INDEX

**TO VOLUMES 1-24
AND
SUPPLEMENT**

A WILEY-INTERSCIENCE PUBLICATION

John Wiley & Sons

NEW YORK • CHICHESTER • BRISBANE • TORONTO • SINGAPORE

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940 Poly(1-vinylpiperazine)

- Poly(1-vinylpiperazine) [40210-44-4]
 - polyblends of, 18:469
- Poly(vinyl pivalate) [26715-88-8], 4:866
- Poly(2-vinylpyridine) [9003-47-8]
 - with $\text{Co}_2(\text{CO})_8$ as oxo catalyst, 16:641
 - dyeing of, 16:362
 - fatty alkyl bromide reaction, 20:226
 - iodine-doped, 18:758
 - in lithium primary batteries, 3:542
 - polyblends of, 18:468, 469
 - semiconductor, 20:687
 - thermal stabilizer, 11:61
 - in tire cords, 23:78
 - TNCQ complex, 18:776
- Poly(4-vinylpyridine) [25232-41-1], 20:226
 - polyelectrolytes, 18:496
 - TNCQ complex, 18:776
- Poly(vinylpyridine) copolymers
 - as magnetic tape binders, 14:741
- Poly(2-vinylpyridine-co-styrene-co-butadiene) [9019-71-0]
 - adhesive with RF, 13:57
- Poly(4-vinylpyridine-co-*n*-vinylpyrrolidinone) [28902-01-4]
 - reduced-nicotinamide polymer from, 24:64
- Poly(vinylpyridinium iodide) [81771-28-0]
 - dopant, 20:688
- Poly(1-vinyl-2-pyrrolidinone) [9003-39-8]
 - in fruit juice mfg, 11:306
- Polyvinylpyrrolidine [9003-43-4]
 - suspending agent, 23:905
- Poly(*N*-vinyl-2-pyrrolidinone) [9003-39-8] (PVP), 23:963, 967
 - in adhesives with polyaziridine, 13:161
 - biodegradability, 5:643
 - in contact lenses, 6:726
 - for eye prostheses, 19:287
 - as flocculant, 10:508
 - in hair sprays, 12:97
 - hollow fibers, 12:501
 - in I_2 antiseptics, 7:803
 - joint lubricant, 19:296
 - manufacture of, 1:268
 - osmosis membranes, 20:241
 - plasma extender, 3:908
 - plasticizers for, 18:165
 - polyblends of, 18:468
 - properties, 20:220
 - in slow-drug-release devices, 17:298
 - as stabilizer, 23:760
 - water-soluble polymers, 5:643
- Poly(*N*-vinyl-2-pyrrolidinone) complex with
 - iodine [25655-41-8]
 - in antimicrobial agents, 13:232
 - disinfectant, 13:674
 - germicidal, 7:168
 - germicide, 23:971
- Poly(*N*-vinyl-2-pyrrolidinone-co-dimethylaminoethyl methacrylate) [30581-59-0], 23:973
- Poly(*N*-vinyl-2-pyrrolidinone-co-ethyl acrylate) [25085-37-4], 23:973
- Poly(vinylpyrrolidinone-*g*-hydroxyethyl methacrylate) [29612-57-5], 6:722, 727
- Poly(vinylpyrrolidinone-co-vinyl acetate) [25086-89-9], 23:972
 - hair-spray resin, 12:97
- Poly(vinylruthenocene) [76082-17-2], 15:188, 195
- Poly(vinylstyrylacrylate), 17:695
- Poly(vinylsulfonic acid) [26101-52-0], 22:244
 - polyelectrolytes, 18:496
- Poly(vinyl toluene) [9017-21-4]
 - thermal stability of, 21:814
 - from toluene, 23:268
- Poly(vinyltoluene-co- α -methylstyrene) [9017-27-0], 12:863
- Poly(vinyltoluene-co- α -methylstyrene-co-styrene) [68425-58-1], 12:864
- Polywax 500 polyethylene, 24:478
- Polywax 2000 polyethylene, 24:478
- Polyweb, 16:78
- Polywet, 20:226
- Poly(*p*-xylene) [25951-90-0], 24:744, 745
 - as liquid crystal, 14:418
 - from *p*-xylene, 24:714
- Polyynes
 - pyrolysis, 18:769
- Pomace
 - from grapes, 24:563
- Pomanders
 - odor modification with, 16:304
- Pomeranchuk effect, 12:257
- Pomeranz-Fritsch synthesis, 19:559
- Ponasterone A [13408-56-5], 21:715
- Ponceau R [3761-53-3], 17:886. (See also *Acid scarlet*.)
- Ponceau 3R [3564-09-8], 6:561
- Ponceau SX [4548-53-2], 6:562
- Ponchon-Savarit diagram, 9:725
- Pondimin, 3:191
- Pond-Maddin technique
 - liquid quenching, 11:905
- Ponds
 - reverse-gradient, 21:303

KIRK-OTHMER

**ENCYCLOPEDIA OF
CHEMICAL TECHNOLOGY**

THIRD EDITION

VOLUME 23

**THYROID AND ANTITHYROID PREPARATIONS
TO
VINYL POLYMERS**

A WILEY-INTERSCIENCE PUBLICATION

John Wiley & Sons

NEW YORK • CHICHESTER • BRISBANE • TORONTO • SINGAPORE

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[25189-83-7], unlike PVP, precipitates from aqueous solution above 30–35°C. It is water soluble, but it is significantly less hygroscopic than PVP at high relative humidity, and is effective as a hairspray resin (34) (see Hair preparations).

Poly(*N*-Vinyl-2-Pyrrolidinone)

Poly(*N*-vinyl-2-pyrrolidinone) (PVP) is undoubtedly the best characterized and most widely studied *N*-vinyl polymer. It derives its commercial success from its biological compatibility, low toxicity, film-forming and adhesive characteristics, unusual complexing ability, and relatively inert behavior toward salts, acids, and thermal degradation in solution. These properties have suggested many medicinal applications.

In the United States, PVP is sold in both pharmaceutical and technical grades. The pharmaceutical grades, known generically as povidone, are marketed under the trade names Plasdone (GAF Corporation) and Kollidon (BASF). The technical grades are manufactured under a variety of names, such as PVP, Peregol ST, Albigen A, and Luviskol. Special cross-linked grades of PVP known as Crospovidone, PVPP, and polyvinylpyrrolidone are sold to the pharmaceutical industry under the trade names Polypasdone XL (GAF) and Kollidon CL (BASF), and to the beer (qv) and wine (qv) industries under the trade name Polyclar.

First developed in Germany at I. G. Farben during the 1930s, PVP was subsequently widely used in Germany as a blood-plasma substitute and extender during World War II. In the United States, it has been manufactured since 1956 by GAF, the sole domestic supplier of PVP. GAF also makes the starting chemicals for its production at Calvert City, Kentucky, and Texas City, Texas; the latter plant became operational in 1969.

Properties. Poly(*N*-vinyl-2-pyrrolidinone) is described in the *United States Pharmacopoeia* (35) as consisting of linear *N*-vinyl-2-pyrrolidinone groups of varying degrees of polymerization. The molecular weights of PVP samples are determined by osmometry, ultra-centrifugation, light-scattering photometry, and solution viscosity techniques (36). The most frequently employed method of determining and reporting the molecular weight of PVP samples utilizes solution viscosity and, therefore, the viscosity-average molecular weight \bar{M}_v is obtained.

A frequently used and commonly recognized method of distinguishing between different molecular weight grades of PVP is the *K* value. Its nomenclature is accepted by the USP, FDA, and other authoritative bodies worldwide. The *K* value is usually determined at 1% wt/vol of a given PVP sample in aqueous solution. The relative viscosity is obtained with an Ostwald-Fenske or Cannon-Fenske capillary viscometer, and the *K* value is derived from Fikentscher's equation (37):

$$\log \frac{\eta_{rel}}{c} = \frac{75 K_o^2}{1 + 1.5 K_o c} + K_o$$

where $K = 1000 K_o$, rel = relative, and c = concentration of the solution in g/100 mL. Solving directly for *K*, the Fikentscher equation is converted to:

$$K = [\sqrt{300 c \log Z + (c + 1.5 c \log Z)^2 + 1.5 c \log Z - c}] / (0.15 c + 0.003 c^2)$$

where $Z = \eta_{rel}$.

The intrinsic viscosity $[\eta]$ is defined as:

$$[\eta] = \lim_{c \rightarrow 0} \left(\frac{\ln \eta_{rel}}{c} \right)$$

and is usually determined by measuring the relative viscosity at a number of concentrations and extrapolating $\ln \eta_{\text{rel}}/c$ to zero concentration. It may, however, be approximated from the Fikentscher equation by:

$$[\eta] = 2.303 (0.001 K + 0.000075 K^2)$$

where $[\eta]$ = intrinsic viscosity and K = K value of sample.

Utilizing the Mark-Houwink equation (38–39):

$$[\eta] = k \bar{M}_v^a$$

where k = the Mark-Houwink constant, it is possible to relate the viscosity-average molecular weight (\bar{M}_v) to the K value.

In the past, the two principal worldwide suppliers of PVP, GAF and BASF, have reported different \bar{M}_v for products with equivalent K values. The difference does not arise from differences in the actual material, but rather from the use of different values for the constants k and a in the Mark-Houwink equation. Previously, GAF employed values for k and a of 1.6×10^{-5} and 0.9, respectively, whereas BASF used the values $k = 1.4 \times 10^{-4}$ and $a = 0.7$. Recently, all manufacturers have elected to adopt the constants $k = 1.4 \times 10^{-4}$ and $a = 0.7$ (38–39). A comparison of the viscosity-average molecular weight for various K -value grades of PVP is given in Table 6. The old values reflect the earlier GAF determinations and the new values reflect the use of recently proposed constants (38–39); the latter are currently used by both GAF and BASF.

Because many earlier disclosures utilized the older GAF determinations of \bar{M}_v , it is suggested that the reader employ the K value when attempting to repeat or verify earlier experiments or formulations. Table 7 lists PVP grades with their K values and calculated \bar{M}_v values.

Table 6. PVP K Values and Viscosity-Average Molecular Weight (\bar{M}_v)

K Value	$[\eta]^a$	Old GAF \bar{M}_v^b	New GAF \bar{M}_v^c
10	0.0403	6,010	3,260
12	0.0525	8,070	4,760
15	0.0734	11,700	7,680
17	0.0891	14,500	10,100
20	0.1151	19,300	14,600
25	0.1655	28,900	24,500
28	0.1999	35,600	32,100
29	0.2120	38,000	34,900
30	0.2245	40,500	37,900
31	0.2373	43,100	41,000
32	0.2505	45,800	44,300
50	0.5469	109,000	135,000
60	0.7599	157,000	216,000
80	1.2894	283,000	460,000
85	1.4434	321,000	541,000
90	1.6061	360,900	630,000
100	1.9572	450,000	836,000

^a $[\eta] = 2.303 (0.001 K + 0.000075 K^2)$.

^b $\bar{M}_v = \left(\frac{[\eta]}{1.6 \times 10^{-5}} \right)^{1/0.9}$

^c $\bar{M}_v = \left(\frac{[\eta]}{1.4 \times 10^{-4}} \right)^{1/0.7}$

Table 7. Viscosity-Average Molecular Weights of Commercial Grades of PVP

Grade	Manufacturer	Calculated \bar{M}_v
<i>Technical</i>		
PVP K-15	GAF	7,680
K-30	GAF	37,900
K-60	GAF	216,000
K-90	GAF	630,000
Luviskol 90	BASF	630,000
Peregal ST, K-30	GAF	37,900
Albigen A, K-30	BASF	37,900
<i>Pharmaceutical</i>		
Plasdone C-15 ^a	GAF	7,680
C-30 ^a	GAF	37,900
K-25	GAF	24,500
K-26/28	GAF	29,400
K-29/32	GAF	40,000
K-90	GAF	630,000
Kollidon K-12 PF	BASF	4,760
K-17 PF	BASF	10,000
K-25	BASF	24,500
K-30	BASF	37,900
K-90	BASF	630,000

^a Pyrogen-free.

Poly(*N*-vinyl-2-pyrrolidinone) is soluble in a variety of organic solvents. The solubility behavior of PVP toward organic solvents is given in Table 8; 5% solutions in heptane, Stoddard's solvent, kerosene, and toluene may be prepared from a 25% solution of PVP in butanol. Solutions in the chlorofluoroalkane propellants can be made by using a 20–30% PVP in ethanol.

Solubility in water is limited only by the viscosity of the resulting solution. The heat of solution is -4.81 kJ/mol (-1.15 kcal/mol) (40); aqueous solutions are slightly acidic (pH 4–5).

Table 8. Solubility of PVP in Organic Solvents

Soluble ^a	Insoluble
alcohols	hydrocarbons
acids	ethers
esters	esters
ethyl lactate	ethyl acetate
ketones	sec-butylacetate
methylcyclohexanone	ketones
chlorinated hydrocarbons	2-butanone
methylene dichloride	acetone
chloroform	cyclohexanone
ethylene dichloride	chlorinated hydrocarbons
amines	chlorobenzene
glycols	
lactams	
nitroparaffins	

^a Minimum of 10 wt % PVP dissolves at room temperature.

Figure 1 illustrates the kinematic viscosity of three grades of PVP in aqueous solution. The kinematic viscosity of PVP K-30 in various organic solvents is given in Table 9. Poly(*N*-vinyl-2-pyrrolidinone) is a gelling agent for polar solvents such as halogenated alkanes, halogenated alkenes, tertiary amines, ketones, and esters when mixed with C_1 - C_5 alcohols (41).

Under ordinary conditions, PVP is stable as a solid and in solution (42). The solid

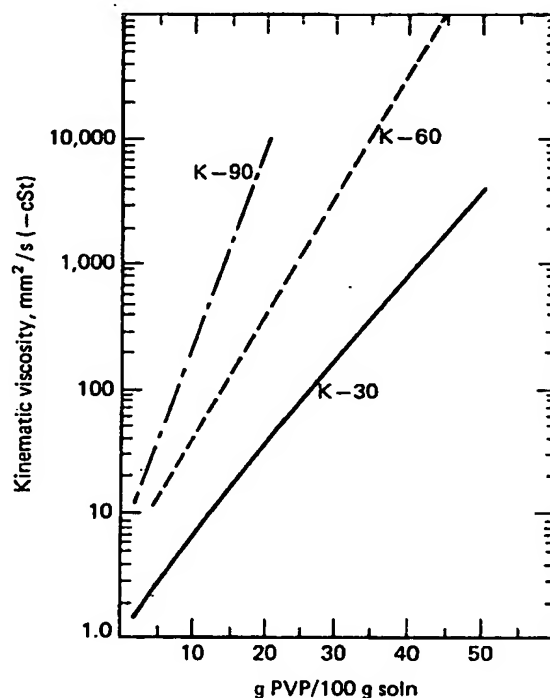


Figure 1. Viscosity of aqueous PVP solutions.

Table 9. Viscosity of PVP K-30 in Organic Solvents

Solvent	2% PVP, mm ² /s (= cSt)	10% PVP, mm ² /s (= cSt)
acetic acid, glacial	2	12
1,4-butanediol	101	425
butyrolactone	2	8
cyclohexanol	80	376
diacetone alcohol	5	22
diethylene glycol	39	165
ethanol, absolute	2	6
ethyl lactate	4	18
ethylene glycol	24	95
ethyl ether	3	12
glycerol	480	2046
2-propanol	4	12
methylcyclohexanone	3	10
<i>N</i> -methyl-2-pyrrolidinone	2	8
methylene dichloride	1	3
nonylphenol	3300	
propylene glycol	66	261
triethanolamine	156	666

tolerates heating in air for 16 h at 100°C, but darkening and loss in solubility occurs at 150°C. At pH 12, the polymer gels irreversibly within four hours at 100°C. In strong acid solution, PVP is unusually stable with no change in appearance or viscosity for two months at 24°C in 15% HCl. Studies of various thickening agents for acid gelling showed only PVP to be stable in 15% HCl at 107°C (43). However, viscosity increases in concentrated hydrochloric acid, and in concentrated nitric acid PVP forms a stable gel (44).

The glass-transition temperature of PVP is 175°C (45). The melt viscosity is too high for typical thermoplastic forming operations.

Films of PVP are clear, transparent, glossy, and hard. They can be cast from water, methyl alcohol, chloroform, or ethylene dichloride. Dried film from PVP K-30 has a specific gravity of $d_4^{25} = 1.25$ and a refractive index of $n_D^{25} = 1.53$ (46). It is comparatively hygroscopic and is between carboxymethyl cellulose (CMC-70) and poly(vinyl alcohol) (PVA) in absorption of water at 30–90% rh, with CMC-70 > PVP > PVA. At 70% rh, PVP films become tacky, and at 50% rh, they contain 18% moisture.

A number of synthetic and natural resins can be combined with PVP to yield clear solutions and films. Among these compatible resins are ethyl cellulose, polyethylene, poly(vinyl chloride), poly(vinyl alcohol), poly(vinyl methyl ether), shellac, corn dextrin, and polyacrylonitrile (1:3) (see also Resins, water-soluble). Incorporation of high molecular weight PVP increases the transparency of polyamides (47) and improves dye receptivity of cellulose derivatives (48). Combinations of cellulose and PVP are also used as hemodialysis membranes (49).

The single most attractive property of PVP is its binding capability. This property has permitted utilization in numerous commercial applications. Small quantities of PVP stabilize aqueous emulsions (qv) and suspensions, apparently by its absorption as a thin layer on the surface of individual colloidal particles. Thus, PVP K-90 is effective in controlling the particle size in the suspension polymerization of styrene (50) and vinyl chloride (51), and it is used as a suspending agent in granulated feed (52). Its suspending ability is a chief reason for its wide use in pill tableting and capsule granulation (53).

Because of its strong complexing ability, PVP improves dye receptivity (48). It stabilizes analytical reagents against oxidation (54). Recent investigations into the nature of the complexation of PVP are contradictory regarding the significance of hydrophobic interactions in the binding of monomolecular species to the polymer (55–57). A loss in complexing ability of PVP occurs at molecular weights of 1000–5000 (57).

A study of the interaction of PVP with albumin and salicylic acid indicates that the PVP reduces the binding of albumin to salicylic acid (58). Poly(*N*-vinyl-2-pyrrolidinone) stabilizes hydrogen peroxide (59). Complexation with PVP controls the release of CO₂ (60). Heavy-metal salt complexes with PVP (61) have been used in computed tomographic (CT) diagnosis of tumors (62) (see Chelating agents; Medical diagnostic reagents; X-Ray technology). The single most widely studied and best characterized PVP complex is that of PVP–iodine [25655-41-8]. Hydrogen triiodide forms a complex with PVP that is so stable that there is no appreciable vapor pressure. It is superior to tincture of iodine as a germicide (63–65) (see Disinfectants and anti-septics).

Polymerization and Manufacture. *N*-Vinyl-2-pyrrolidinone (VP) is readily polymerized with cationic, eg, boron trifluoride (21), or anionic initiators, eg, potassium amide (66) and alkali metals and their oxides (67). Anionic initiators yield a cross-linked polymer which is insoluble in water, strong mineral salts, caustic, and organic solvent. It is sold as Polyclar to the beverage trade where it is used as a clarifier, and to the pharmaceutical trade as Polyplasdone, a tablet disintegrant.

Poly(*N*-vinyl-2-pyrrolidinone) is manufactured by bulk, solution, or suspension polymerization under free-radical catalysis. Bulk polymerization was first employed in the FRG with hydrogen peroxide as catalyst. The reaction is highly exothermic, the temperature rises rapidly from 110 to 190°C and leads to discoloration (46). Therefore, this process was subsequently refined using a 30% aqueous solution of *N*-vinyl-2-pyrrolidinone catalyzed by 0.2% hydrogen peroxide and 0.1% ammonia (46). The rate expression (68) for this polymerization is

$$\text{rate} = k [\text{HOOH}]^{1/2} [\text{NH}_3]^{1/4} [\text{VP}]^{3/2}$$

The rate of polymerization is proportional to the VP concentration up to 50%; beyond 60%, the rate falls off rapidly. The polymerization is relatively insensitive to pH in the range 7–12. Above pH 12, the rate slows and above 13 it is inhibited. The molecular weight of the polymer increases with the VP concentration up to 30%.

In polymerization between 40 and 70°C catalyzed with azobisisobutyronitrile, the rate of propagation (K_p) is expressed as $K_p = 1.87 \times 10^3 \times C^{-7100/RT}$ and the rate of termination (K_t) is expressed as $K_t = 1.00 \times 10^9 \times C^{-1600/RT}$ (69). Studies with various solvents indicate that the energies of termination and propagation differ significantly and are related to the complex formation between the VP and the solvent (see Table 10) (70).

A kinetic study of VP polymerization in aqueous medium showed an interaction energy of ca 8 kJ/mol (1.9 kcal/mol), which indicates a weak hydrogen bond. Hydrogen bonding interactions between water and VP apparently increases the reactivity of VP. This influence is exerted up to a ratio of 75:25 VP:H₂O by volume or a 1:2 molar ratio of VP:H₂O. More water acts as diluent, retards the propagation rate, and has no influence on \bar{M}_v (71).

N-Vinyl-2-pyrrolidinone has been copolymerized with a variety of comonomers in both solution and emulsion systems (see Table 11). The reactivity ratios and propensity to copolymerize may be significantly affected by the solvent (72).

A number of *N*-vinyl-2-pyrrolidinone–vinyl acetate (VA) copolymers [25086-89-9] are marketed as hairspray resins, tablet excipients, and adhesives. The water solubilities of these resins increase with the VP–VA ratio (see Table 12).

Poly(*N*-vinyl-2-pyrrolidinone) has been used to form graft copolymers by poly-

Table 10. Termination and Propagation Activation Energies for 50% VP Solutions

Solvent	Energy of termination, kJ/mol ^a	Energy of propagation, kJ/mol ^a
water	19	68
isopropyl alcohol	13	40 ± 2
methanol	9	32 ± 3
ethyl acetate	8	23

^a To convert J to cal, divide by 4.184.

Table 11. Reactivity Ratios (r_1 and r_2) for Free-Radical Copolymerization of *N*-Vinyl-2-pyrrolidinone (M_1)^a

Comonomer (M_2)	r_1	r_2
acrylonitrile	0.06 ± 0.07	0.18 ± 0.07
allyl alcohol	1.0	0.0
allyl acetate	1.6	0.17
allylidene diacetate	0.92	0.94
crotonic acid ^b	0.85	0.02
maleic anhydride	0.16 ± 0.03	0.08 ± 0.03
methyl methacrylate	0.005 ± 0.05	4.7 ± 0.05
trichloroethylene	0.54 ± 0.04	<0.01
tris(trimethylsiloxy)vinylsilane	4.0	0.1
vinyl chloride	0.38	0.53
vinyl cyclohexyl ether	3.84	0.0
vinyl phenyl ether	4.43	0.22
vinylene carbonate	0.4	0.7

^a From ref. 72, except where otherwise indicated.^b From ref. 73.

Table 12. VP-Vinyl Acetate Copolymers

Designation				
BASF	GAF	VP, %	VA, %	Solvent
	PVP/VA E-335	30	70	ethanol
	PVP/VA E-535	50	50	ethanol
	PVP/VA E-635	60	40	ethanol
	PVP/VA E-735	70	30	ethanol
Luviskol VA-37	PVP/VA I-335	30	70	2-propanol
	PVP/VA I-535	50	50	2-propanol
	PVP/VA I-735	70	30	2-propanol
Luviskol VA-64 ^a	PVP/VA S-630	60	40	

^a Powder.

merization techniques (74–76). The graft copolymers are available as latices from GAF under the trade name Polecron; polymers [25085-37-4] of PVP with ethyl acrylate are Polecron 130 and, with vinyl acetate, Polecron 8252 and 9452. These copolymers are compatible with synthetic and natural resins and impart oil and grease resistance, dye receptivity, improved machining qualities, and increased adhesion to a number of substrates. They are typically employed in the adhesives, cleaning agents, textile, paper, particle-binder, leather, metal, and cosmetic industries. Alternatively, alkylated homopolymers may be obtained by grafting an alkyl group onto PVP (77) and functional polymers by the simultaneous polymerization and aminoalkylation of *N*-vinyl-2-pyrrolidinone (78). These alkylated *N*-vinyl-2-pyrrolidinones, exemplified by Ganex V-516 [53240-90-7], are suspending aids in the paint, radiation-curing, and polymerization industries, in both aqueous and solvent medium. Gafquat 734 and 755N, copolymers [30581-59-0] of *N*-vinyl-2-pyrrolidinone and dimethylaminoethyl methacrylate, are widely used as additives in hair-care products.

Specifications and Analysis. The specifications for technical and pharmaceutical grades of PVP are given in Tables 13 and 14.

In powders, moisture content is determined by Karl Fischer reagent; the Cenco moisture balance is used with aqueous solutions. Residual *N*-vinylpyrrolidinone is determined by iodometric titration; ash by ignition; heavy metals by spectrographic emission; arsenic by standard USP method; nitrogen by Kjeldahl or Dumas methods; and acetaldehyde by hydroxylamine method. The *K* value is measured as specified by the second supplement of the USP (35).

Health and Safety Factors. The acute oral lethal dose (LD₅₀) of PVP K-30 is reported to be >100 g/kg. It is not a skin or eye irritant, or a skin sensitizer. Toleration of PVP K-30 is good by intraperitoneal, intramuscular, and intravenous routes. Its use as a plasma volume expander is predicated on this tolerance. Cancer occurrence in humans has not been demonstrated for assimilation of any molecular weight of PVP by any route.

Apparently, PVP is not absorbed from the gastrointestinal tract. Studies of intravenous application indicate that the lower molecular weight material is readily excreted through the kidneys; higher molecular weight material is more slowly eliminated. Poly(*N*-vinyl-2-pyrrolidinone) with molecular weights over 100,000 is not readily removed and apparently is phagocytized by the cells of the reticuloendothelial system and deposited in storage sites in the liver, spleen, lung, etc. Such storage usually is not associated with pathological changes.

Table 13. Specifications of Technical PVP Grades

Designation	Form	<i>K</i> range	Water, % max	Ash, % max	Residue monomers, % max
PVP K-15	powder	12-18	5	0.02	1.0
PVP K-30	powder	26-35	5	0.02	1.0
PVP K-60	aqueous solution	50-62	55	0.02	1.0
PVP K-90	aqueous solution	80-100	80	0.02	1.0
PVP K-90	powder	80-100	5	0.02	1.0
Polyclar AT	powder	cross-linked	5		

Table 14. Specifications of Pharmaceutical PVP Grades

Assay	Value
<i>K</i> value	
10-15	85-115% of stated value
16-90	90-107% of stated value
moisture, % max	5
pH ^a	3.0-7.0
residue on ignition, %, max	0.02
aldehydes, % ^b , max	0.02
<i>N</i> -vinyl-2-pyrrolidinone, %, max	0.20
lead, ppm, max	10
arsenic, ppm, max	1
nitrogen, %	11.5-12.8

^a Of a 5% solution in distilled water.

^b Calculated as acetaldehyde.

Uses. Cosmetics and Toiletries. Poly(*N*-vinyl-2-pyrrolidinone) and its copolymers are widely used in the hair- and skin-care industries, not merely as additives but as an integral part because of their nontoxic and sorptive behavior as well as emulsifying, thickening, emollient, and dye-solubilizing abilities (see also Cosmetics; Hair preparations).

Photographic Industry. Poly(*N*-vinyl-2-pyrrolidinone) acts as a protective colloid (79) and silver halide suspending agent (80). More recently, it has been claimed as a processing aid in the development of silver halide film and is used to eliminate the occurrence of dichroic stain (81). As a coating aid, PVP in silver halide emulsions reduces viscosity and increases the covering power of the developed image (82) (see also Photography).

Oil-Recovery Industry. Poly(*N*-vinyl-2-pyrrolidinone) is useful in various areas of oil recovery (see Petroleum, chemicals for enhanced recovery). It has been employed as an additive to cement formulations to increase viscosity and setting time while decreasing fluid loss (83–84) (see Cement).

It is an exceptionally stable acid-gelling agent for acid fracturing (43,85–91). Because of its relative insensitivity to salt concentration and environmental degradation, PVP has been claimed as a valuable tool in polymer flooding using high salt concentrations in areas containing water-sensitive clays (92–93). Studies of PVP in the area of surfactant flooding indicate that injection of an aqueous solution of PVP into the formation before injection of the surfactant greatly reduces the loss of the surfactant by adsorption on the formation (94).

Textiles. Incorporation of PVP into hydrophobic fibers such as polyacrylonitrile (95–96), polyesters (97–98), nylon (99–100), and cellulosic material (48) greatly increases their dyeability. Poly(*N*-vinyl-2-pyrrolidinone) has also been utilized as an anti-soil-redeposition agent (101–103), stripping agent (104), and pigment-shock reducer (105). Graft copolymers of PVP with nylon (57) exhibit improved wet-crease recovery and moisture regain (106–107).

Detergents. Poly(*N*-vinyl-2-pyrrolidinone) is compatible in clear, liquid, heavy-duty detergent formulations (108). It has been formulated with borax in a pretreat washing formulation (109). Owing to its detoxifying behavior, it is utilized as an essential component in formulations containing phenolic sanitizer cleaners.

Beverages. The ability of PVP to complex with certain polyphenolic compounds (tannins and others) has led to its use in the clarification and chillproofing of fruit beverages (110–111). The addition of 0.01–0.02% of soluble PVP to the brew kettle improves taste and reduces chill haze (112–113). Poly(*N*-vinyl-2-pyrrolidinone) is similarly employed in wines (114), vinegar, etc (115).

Pharmaceuticals. The lack of toxicity and high solubility of poly(*N*-vinyl-2-pyrrolidinone) have made it ideally suited for a number of pharmaceutical applications. Special grades of pyrogen-free PVP are marketed under the label Plasdone C and are available in K-15 (\bar{M}_v 8000) and K-30 (\bar{M}_v 38,000) molecular weights.

Poly(*N*-vinyl-2-pyrrolidinone) was first employed as a blood extender during World War II. It is nonantigenic, requires no cross-matching, and avoids the danger of infectious diseases inherent in blood.

As a tablet binder, PVP's solubility in both aqueous and organic solvents enables it to be used in virtually all formulations (116). The combination of high solubility and workable viscosities, enables the reduction of the volume of granulating solution, resulting in decreased drying times and cost. Moisture-sensitive drugs can be suc-

cessfully granulated by utilizing PVP in anhydrous solvent (117). Water-soluble PVP (eg, Plasdone) can be dry-blended with the powder mix and then wetted with an appropriate solvent during granulation. The use of PVP aids in the production of free-flowing, compressible granulation which produces hard tablets with good dissolution rates. It is also used in sustained-release formulations. Poly(*N*-vinyl-2-pyrrolidinone) has also found wide acceptance as an ingredient in aqueous and solvent-based tablet-coating solutions. It improves the adhesion of the film to the tablet surface; modifies the disintegration times of films based on hydrophobic materials; acts as a plasticizer, stabilizer, and dispersant; and increases the spreadability of pigment-containing solutions.

An important application is derived from the ability to complex and solubilize poorly soluble drugs and hence increase their bioavailability and efficiency. Poly(*N*-vinyl-2-pyrrolidinone) is coprecipitated with a hydrophobic drug by dissolving both in a common solvent and then evaporating to dryness. The resulting complex is powdered and formulated in a dosage form. A wide number of drugs have been formulated in this manner (118–125). Alternatively, drugs with poor water solubility may be prepared as aqueous solutions by dissolving or suspending the drug in aqueous solutions of PVP (116). In tablet formulations, PVP increases the stability of certain drugs. For example, it decreases the volatility in nitroglycerin and the hydrolysis of aspirin (88–90).

Highly cross-linked poly(*N*-vinyl-2-pyrrolidinone), generically termed Crospovidone, N.F., and sold in the United States as Polyplasdone XL (GAF), is a tablet excipient. It is a water-insoluble but still highly hydrophilic form of the polymer, which is utilized in both wet and direct compression tableting. When exposed to water, this PVP swells and causes high stress on the surrounding tablet components and rapid disintegration (126).

A recent advance in medical technology is the development of transdermal application, which utilizes patches containing drugs capable of being absorbed through the skin. One such system employs nitroglycerin for the treatment of angina pectoris (127). Poly(*N*-vinyl-2-pyrrolidinone) is used as a binder to create a gel-like matrix for the drug, facilitating diffusion (see Pharmaceuticals, controlled release).

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